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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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ROBINS & PASTERNAK
1731 EMBARCADERO ROAD
SUITE 230
PALO ALTO, CA 94303

EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/996,484	CHOO ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7,8,10,11,13-15,21-26,31,34,35 and 38-49* is/are pending in the application.

4a) Of the above claim(s) *1,2,4,5,8,10,11,13-18,21-26,31 and 38-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,48 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 17 February 2006 has been entered.

This Office Action is a reply to the 17 February Paper filed in response to the Final Office Action mailed 15 November 2005. Claims 1, 2, 4, 5, 8, 10, 11, 13-18, 21-26, 31, 38-47 were withdrawn from consideration and claim 34 was considered in the 15 November Office Action. Claim 34 was amended and claims 48 and 49 were added in the 17 February Paper. Claims 1, 2, 4, 5, 7, 8, 10, 11, 13-15, 21-26, 31, 34, 35 and 38-49 are pending and claims 34, 48 and 49 are under consideration.

Response to Amendment and Arguments

Claim Rejections - 35 USC § 101

Rejection of claim 34 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is **withdrawn** in view of the amendment of the claim such that the molecular switch is now limited to comprising a polypeptide comprising a non-naturally occurring Cys2-His2 zinc finger binding domain.

Claim Rejections - 35 USC § 102

Rejection of claim 34 under 35 U.S.C. 102(b) as being anticipated by any one of Porter *et al.* (1997) *Mol. Endocrinol.* 11:1569-1580 as evidenced by Pratt *et al.* (1997) *Endocrine Rev.* 18:306-360 (the discussion of Porter *et al.* will refer to the HTML version of the article mailed herewith), Kobayashi *et al.* (1996) *J. Biol. Chem.* 271:12310-12316 or Perkins *et al.* (1993) *EMBO J.* 12:3551-3558 as evidenced by the Prosite Database entry PDOC00028, "Zinc finger C2H2-type domain signature and profile", available at us.expasy.org/cgi-bin/prosite-search-ac?PDOC00028 is **withdrawn** in view of the amendment of the claim such that the molecular switch is now limited to comprising a polypeptide comprising a non-naturally occurring Cys2-His2 zinc finger binding domain.

New Grounds

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 49 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The new claim, as written, does not sufficiently distinguish over switching systems that exist naturally (*e.g.*, estrogen receptor/Sp1/estrogen; see the discussion under "Claim Rejections - 35 USC § 102" herein below) because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. Although the claim recites that the switching system comprises a "polypeptide

compris[ing] a mutant zinc finger protein" the process of mutation occurs naturally and essentially all proteins have evolved through a process involving mutation. The specification does not provide a limiting definition of the claim limitation that would exclude natural mutants and there is no clear benchmark standard of a "non-mutant zinc finger protein" that would exclude natural mutations from the scope of the claim. Therefore, naturally occurring switching systems comprising zinc finger proteins comprising mutations relative to their evolutionary precursors are within the scope of the claims. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor. See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 34 is indefinite in reciting that a polypeptide comprises a "non-naturally occurring Cys2-His2 zinc finger binding domain". The specification states, "The term 'a non-naturally occurring binding domain' means that the binding domain does not occur in nature, even as a part of a larger molecule" (page 3, lines 29-31). Thus, the claim limitation requires that zinc finger binding domain does not occur in nature. However, proteins in nature are polymorphic as

a consequence of continual mutation and the full scope of zinc finger domains occurring in nature is unknown. Even if a zinc finger domain is subject to deliberate mutagenesis in the laboratory, the skilled artisan would not know if the mutagenized zinc finger domain is "non-naturally occurring" and therefore within the scope of the claim limitation, because the scope of zinc finger domains occurring in nature is unknown. In other words, the scope of the claim limitation is indefinite because the benchmark used to determine whether any given zinc finger domain is "non-naturally occurring" is unknown and unknowable.

Claim 49 is indefinite in reciting that a polypeptide comprises "a mutant zinc finger protein". The term "mutant" is relative and, therefore, assessing the metes and bounds of the limitation requires a clear benchmark. For example, if two allelic variants of a protein are known, which protein is mutant and which is non-mutant? It is impossible to know unless the sequence of the "non-mutant" protein is clearly defined. As the application does not set forth a limiting definition of "mutant" and the claim fails to set forth a standard by which the mutant or non-mutant character of a given protein is determined, the metes and bounds of the claim as a whole are unclear. In view of the absence of any objective standard to determine whether a given protein is "mutant" and the fact that all proteins have evolved through a process of mutation, the "mutant zinc finger protein" of the claims is broadly construed as encompassing all zinc finger proteins.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 49 is rejected under 35 U.S.C. 102(b) as being anticipated by any one of Porter *et al.* (1997) *Mol. Endocrinol.* 11:1569-1580 as evidenced by Pratt *et al.* (1997) *Endocrine Rev.* 18:306-360 (the discussion of Porter *et al.* will refer to the HTML version of the article mailed herewith), Kobayashi *et al.* (1996) *J. Biol. Chem.* 271:12310-12316 or Perkins *et al.* (1993) *EMBO J.* 12:3551-3558 as evidenced by the Prosite Database entry PDOC00028, "Zinc finger C2H2-type domain signature and profile", available at us.expasy.org/cgi-bin/prosite-search-ac?PDOC00028.

As state above, in view of the absence of any objective standard to determine whether a given protein is "mutant" and the fact that all proteins have evolved through a process of mutation, the "mutant zinc finger protein" of the claims is broadly construed as encompassing all zinc finger proteins including the Sp1 protein found in nature.

Porter *et al.* teaches, "cooperative interactions of Sp1 and ER proteins play a role in regulation of at least five estrogen inducible genes, including c-*myc*, *CKB*, cathepsin D, RARα, and Hsp27" (page 3 of 12, lines 9-11). In Figure 2, Porter *et al.* demonstrates estrogen-induced expression from a reporter gene construct comprising an Sp1 binding site in cells cotransfected with an estrogen receptor and in Figure 8 Porter *et al.* demonstrates specific protein-protein interaction of the estrogen receptor with Sp1. In sum, Porter *et al.* teaches a switching system comprising a first polypeptide (*i.e.*, an estrogen receptor) and a second polypeptide (*i.e.*, Sp1) and a ligand (*i.e.*, estrogen). Although Porter *et al.* teaches that the interaction of the estrogen receptor with Sp1 *in vitro* does not require estrogen (final sentence on page 8 of 12). Pratt *et al.*

teaches that the estrogen receptor is regulated by being held inactive in a complex including hsp90 and that binding of estrogen promotes dissociation of estrogen receptor from the complex and a conversion of the receptor to the DNA binding state (see especially the second full paragraph in the right column on page 343 as well as the paragraph bridging pages 307-308 through the paragraph bridging the left and right columns on page 308). In view of this and the showing of estrogen induced reporter gene expression in the intact cell discussed above, the skilled artisan would view the interaction of the estrogen receptor and Sp1 in the cell as "modulatable by a ligand". Of course, the estrogen receptor is a DNA binding protein (see, *e.g.*, Pratt *et al.*, page 308, paragraph bridging the left and right columns) and Sp1 is a DNA-binding transcription factor which comprises a Cys2-His2 zinc finger (see Prosite entry PDOC00028, the fourth bullet on page 2 of 4). Thus, the switching system of Porter *et al.* comprises each of the limitations of the switching system of the instant claims. Therefore, the claims are anticipated by Porter *et al.* as evidenced by Pratt *et al.* and Prosite Database entry PDOC00028.

Kobayashi *et al.* teaches cotransfection of SL2 cells with a reporter construct comprising a *CYP1A1* promoter and expression constructs encoding transcription factors AhR, Arnt and Sp1, and demonstrates a dramatic increase in reporter gene expression in response to the addition of the inducer molecule 3-MC (see especially the first paragraph in the left column on page 12312 and Figure 1B lanes 7 and 8). In addition, Kobayashi *et al.* demonstrates that the induction is much less in the absence of Sp1 or Ahr/Arnt (Figure 1B, lanes 3-6). Furthermore, Kobayashi *et al.* demonstrate the physical interaction of Sp1 protein with AhR and Arnt in immunoprecipitation experiments (see especially the first full paragraph in the right column on

page 12313 and Figure 4 and the caption thereto) and provide DNaseI footprinting data which suggest the interaction of AhR-Arnt and Sp1 bound to DNA (see especially the paragraph bridging pages 12314-12315 and Figure 8 and the caption thereto). In sum, Kobayashi *et al.* teaches a switching system comprising a first polypeptide (*i.e.*, Ahr/Arnt) and a second polypeptide (*i.e.*, Sp1) and a ligand (*i.e.*, 3-MC). Furthermore, Kobayashi *et al.* teaches that the heterodimeric Ahr/Arnt complex is regulated in a manner similar to steroid hormone receptors, wherein Ahr exists in the cytoplasm bound to hsp90 and is translocated to the nucleus upon binding to inducer (see especially page 12310, left column, lines 8-18). Therefore, the interaction of the Ahr/Arnt with Sp1in the cell is modulatable by a ligand. In addition, Kobayashi *et al.* teaches that the Ahr/Arnt complex is DNA binding (*i.e.*, binds to the xenobiotic responsive element; see especially page 12310, left column, lines 8-19) and Prosite entry PDOC00028 teaches that Sp1 is a DNA-binding transcription factor which comprises a Cys2-His2 zinc finger (*Id.*). Thus, the switching system of Kobayashi *et al.* comprises each of the limitations of the switching system of the instant claims. Therefore, the claims are anticipated by Kobayashi *et al.* as evidenced by Prosite Database entry PDOC00028.

Perkins *et al.* teaches transfection of Jurkat cells with a reporter construct comprising a minimal NFκB/Sp1 enhancer and demonstrate that the Sp1 binding site is required for induction of the promoter by TNFα and PMA (inducers of NFκB; see especially the paragraph bridging the left and right columns on page 3554, Figure 3 and the caption thereto). In addition, Perkins *et al.* provides DNaseI footprinting and cross-linking data, which suggest direct protein-protein interaction of NF-κB and Sp1 (see especially the first full paragraph on page 3554, Figure 2 and

the caption thereto). This interaction is further evidenced by *in vivo* experiments which demonstrate that the TNFα and PMA induced expression require the close juxtaposition of the κB and Sp1 elements (see especially Figure 1B) and require that the elements be in a specific orientation with respect to one another (see especially Figure 4A and the discussion in the left column on page 3554, lines 18-36). In sum, Perkins *et al.* teaches a switching system comprising a first polypeptide (*i.e.*, NF-κB) and a second polypeptide (*i.e.*, Sp1) and a ligand (*i.e.*, TNFα or PMA). Furthermore, Perkins *et al.* teaches that NF-κB is regulated in a manner similar to steroid hormone receptors, wherein NF-κB exists in a covert cytoplasmic form bound to an inhibitory protein IκB and treatment of cells with inducers such as TNFα and PMA results in release of NFκB into the nucleus and stimulation of NF-κB DNA binding (see especially the second full paragraph in the left column on page 3551). Therefore, the interaction of the NFκB with Sp1 in the cell is modulatable by a ligand. In addition, Perkins *et al.* teaches that NF-κB is DNA binding (*i.e.*, binds to the κB element; see especially the second full paragraph in the left column on page 3551 and the paragraph bridging pages 3551-3552) and Prosite entry PDOC00028 teaches that Sp1 is a DNA-binding transcription factor which comprises a Cys2-His2 zinc finger (*Id.*). Thus, the switching system of Perkins *et al.* comprises each of the limitations of the switching system of the instant claims. Therefore, the claims are anticipated by Perkins *et al.* as evidenced by Prosite Database entry PDOC00028.

As the art teaches switching systems comprising all of the elements of the switching system presently claimed, the claim is anticipated by the art and properly rejected under 35 USC §102(b).

Claims 48 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Liden *et al.* (1997) *J. Biol. Chem.* 272:21467-21472 as evidenced by McEwan *et al.* (1996) *BioEssays* 19:153-160 (previously made of record) and Bledsoe *et al.* (2002) *Cell* 110:93-105.

The claims are directed to a switching system comprising a first and second polypeptide and a ligand, wherein the first and second polypeptides bind to each other in a manner modulatable by the ligand, wherein the first and second polypeptide bind to DNA and wherein the first or second polypeptide comprises an engineered zinc finger binding domain or comprises a mutant zinc finger protein.

Liden *et al.* teaches the production of various glucocorticoid receptor mutants comprising engineered DNA binding domains (see especially p. 21468, col. 2, ¶2, Figure 1 and the caption thereto). Linden *et al.* further teaches expressing the mutant glucocorticoid receptors in COS-1 cells and exposing the cells to the glucocorticoid receptor ligand dexamethasone. As discussed in previous Office Actions, McEwan *et al.* describes in detail the DNA binding domain comprised within the glucocorticoid receptor protein (see especially p. 3, Figure 4 and the caption thereto). Also illustrated in Figure 4 of McEwan *et al.* is the binding of the glucocorticoid receptor to DNA as a homodimer. Bledsoe *et al.* teaches, "[h]ormone binding initiates the release of chaperone proteins from the GR, allowing dimerization and translocation of the receptor into the nucleus" (second full paragraph in the right column on page 93). Thus, the glucocorticoid receptor switching system of Liden *et al.* comprises a first and second polypeptide component which both bind to DNA and the ligand, wherein the first polypeptide binds to the second polypeptide in a manner modulatable by a ligand and the ligand (*i.e.*, dexamethasone).

Furthermore, the switching system of Liden *et al.* comprises glucocorticoid receptors comprising engineered zinc finger binding domains. *Id.*

Thus, the switching system of Liden *et al.* comprises each of the elements of the switching system of claims 48 and 49 and the claims are properly rejected under 35 USC §102(b) as anticipated by the art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vegeto *et al.* WO 93/23431 as evidenced by McEwan *et al.* (*supra*) and Bledsoe *et al.* (*supra*) in view of Liu *et al.* (1997) *Proc. Natl. Acad. Sci. USA* 94:5525-5530.

The limitations of claims 48 and 49 are described herein above. Claim 34 is directed to a switching system comprising a first and second polypeptide and a ligand, wherein the first and second polypeptides bind to each other in a manner modulatable by the ligand, wherein the first and second polypeptide bind to DNA and wherein the first or second polypeptide comprises a non-naturally occurring Cys2-His2 zinc finger binding domain.

Vegeto *et al.* teaches mutated steroid hormone receptors and their use as a molecular switch for regulating expression of a nucleic acid in mammals (see especially the Abstract and the discussion commencing p. 6, ¶4 and continued through p. 7, ¶4). Vegeto *et al.* further contemplates steroid hormone receptors such as glucocorticoid receptors as among those to be used as the starting material for constructing the molecular switch (see especially p. 8, ll. 25-28). Thus, Vegeto *et al.* teaches a switching system comprising a first and second polypeptide and a ligand, wherein the first and second polypeptides bind to each other in a manner modulatable by the ligand (as evidenced by the teachings of McEwan *et al.* and Bledsoe *et al.*). Furthermore, Vegeto *et al.* teaches that ligand activated dimerization is a general property of steroid hormone receptors (see especially the paragraph bridging pages 1-2).

Vegeto *et al.* does not teach that a protein should comprise a non-naturally occurring Cys2-His2 zinc finger binding domain or an engineered or mutated zinc finger binding domain.

However, Vegeto *et al.* does teach, "In preferred embodiments of the molecular switch, the modified steroid receptor has both the ligand binding domain and DNA binding domain replaced" (p. 7, ll. 7-9; emphasis added) and suggests certain non-mammalian DNA binding domains.

Liu *et al.* teaches the design and construction of highly selective six finger DNA binding proteins by modification of the Cys2-His2 zinc finger domains of Zif268 and Sp1 proteins (see especially p. 5528, ¶1) and demonstrates that the polydactyl protein can bind to a contiguous 18-bp DNA sequence with high affinity and specificity (see especially Figure 2 and the caption thereto and the section entitled "Characterization of Affinity and Specificity of Two Six-Finger Proteins" commencing on page 5528). The polydactyl zinc finger proteins are also demonstrated to function in human cells to activate or repress transcription (see especially Figure 4 and the caption thereto and the section entitled "Transcriptional Activation and Repression" commencing on page 5528). Liu *et al.* further teaches that such polydactyl zinc-finger proteins should be broadly applicable as genome-specific transcriptional switches in gene therapy strategies and the development of novel transgenic animals, which uses are the same as the uses contemplated by Vegeto *et al.* for the molecular switch described therein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the molecular switch of Vegeto *et al.* to include the engineered polydactyl Cys2-His2 zinc finger DNA binding domain of Liu *et al.* Motivation to combine these teachings comes from the nature of the problem to be solved by the molecular switch of Vegeto *et al.*, which is to regulate expression of a nucleic acid in mammals (*Id.*) and from the teachings of Liu *et al.* that: a) specific delivery of a DNA-binding protein to a single site within a genome as

complex as that found in humans, 3.5 billion bp, requires an address of at least 16 bp (p. 5525, bridging col. 1-2); b) although natural proteins containing long polydactyl arrays of zinc-finger domains have been inferred from sequence, no zinc-finger proteins have been demonstrated to bind such a long contiguous DNA sequence (p. 5525, bridging col. 1-2); and c) the polydactyl proteins described therein can bind to a contiguous 18-bp DNA sequence with high affinity and specificity and function in human cells to activate or repress transcription. Viewed as a whole, the skilled artisan would clearly be motivated to substitute the polydactyl DNA binding domain of Liu *et al.* for the DNA binding domains contemplated by Vegeto *et al.* for construction of a molecular switch operative in mammalian cells to obtain the expected benefit of highly specific delivery of the switch in the complex mammalian genome.

Absent evidence to the contrary, one would have a reasonable expectation of success in combining these teachings in view of the modular nature of steroid hormone receptor proteins (see especially Vegeto *et al.*, p. 2, ¶1) and the demonstration by Liu *et al.* that the DNA binding domains disclosed therein can be fused to heterologous polypeptides and are active in mammalian cells (see especially Figure 1 and the caption thereto).

In view of these considerations, the invention of claims 34, 48 and 49, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC §103(a) as obvious over the art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Daniel M. Sullivan, Ph.D.
Primary Examiner
Art Unit 1636